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FAX COVER SHEET

From: Dr Michael R. Hutchins
To: European Patent Office – Munich
Attention:
Date: 24 July 2006
Subject: EPA 04806258.2
Astex Therapeutics Limited
Our Reference: AST20 (EP)
Number of pages: 25 (including this page)

Dear Sirs,

We enclose herewith a letter and enclosures for bringing the above PCT application into the European regional phase.

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The European Patent Office
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23 July 2006

VIA FACSIMILE - ORIGINAL BY POST

Dear Sirs,

**Re: European Patent Application No. 04806258.2
Derived from International Application No. PCT/GB2004/005464
International Publication No. WO 2005/061463
Applicants: (1) Astex Therapeutics Limited (2) Cancer Research Technology Limited &
(3) The Institute of Cancer Research: Royal Cancer Hospital
Representative's Reference: AST20(EP)/MRH**

We file herewith the following items in order to bring the above International application into the European Regional Phase.

1. A form 1200
2. Replacement pages 201 to 216 containing an amended set of claims which should form the basis for the further examination of this application.
3. A form 1037 for acknowledging safe receipt of this letter and the enclosures.

For the avoidance of doubt, we note that all amendments made at this stage are without prejudice to the later reinstatement of any deleted subject matter or the filing of a divisional application thereto.

The enclosed form 1200 contains a request for the fees due on this application to be debited from our deposit account by means of the automatic debiting procedure. However, if any further authorisation is needed, we request that this letter be taken as the necessary authorization to debit the deposit account of M.R. Hutchins & Co. (Deposit account no. 28050421) in respect of any outstanding fees.

A form 1037 is enclosed.

Yours faithfully

M. R. HUTCHINS & CO



Dr Michael R. Hutchins

Authorized Representative

Proprietor: Michael R. Hutchins PhD, CPA, EPA, RTMA

Assisted by: Christine E. Hutchins BSc

Records: Sarah Chapman Consultant: Vincent A. Price PhD, EPA, ETMA



Europäisches Patentamt

European Patent Office

Office européen des brevets

Einsender / Sender / Expéditeur :

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 Europäischen Patentamt**

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Eingereichte Unterlagen

Items filed

Pièces envoyées

Anmeldungs- (und Direktions-*) Nr./Patent Nr. Application (and Directorate*) No./Patent No. N° de la demande (et de la direction*)/n° du brevet	Ihr Zeichen Your reference Votre référence	ggfs. Art und Datum der Unterlagen** Nature and date of items (optional)** Nature et date des pièces (facultatif)**
1 EPA 04806258.2	AST20 (EP)	(i) letter dated 24.7.2006
2		(ii) pages 201-216
3		(iii) form 1200
4		
5		
6		
7		
8		
9		
10		

* falls bereits bekannt
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Europäisches Patentamt

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Einsender / Sender / Expéditeur:

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Eingereichte Unterlagen

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1	EPA 04806258.2	AST20 (EP)	(i) letter dated 24.7.2006
2			(ii) pages 201-216
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An das Europäische Patentamt

To the European Patent Office

A l'Office européen des brevets



**Eintritt in die
europäische Phase
(EPA als Bestimmungsamt
oder ausgewähltes Amt)**

**Entry into the
European phase
(EPO as designated or
elected Office)**

**Entrée dans la
phase européenne
(l'OEB agissant en qualité
d'office désigné ou élu)**

Europäische Anmeldenummer oder, falls nicht bekannt, PCT-Aktenzeichen oder PCT-Veröffentlichungsnummer

WO 2005/061463

European application number, or, if not known, PCT application or publication number

04806258.2

Numéro de dépôt de la demande de brevet européen ou, à défaut, numéro de dépôt PCT ou de publication PCT

PCT/GB2004/005464

Zeichen des Anmelders oder Vertreters (max. 15 Positionen)

Applicant's or representative's reference (max. 15 spaces)

Référence du demandeur ou du mandataire (15 caractères ou espaces au maximum)

AST20 (EP)

1. Anmelder

Die Angaben über den (die) Anmelder sind in der internationalen Veröffentlichung enthalten oder vom Internationalen Büro nach der internationalen Veröffentlichung vermerkt worden.



Änderungen, die das Internationale Büro noch nicht vermerkt hat, sind auf einem Zusatzblatt angegeben.



Zustellanschrift
(siehe Merkblatt II, 1)

1. Applicant

Indications concerning the applicant(s) are contained in the international publication or recorded by the International Bureau after the international publication.

Changes which have not yet been recorded by the International Bureau are set out on an additional sheet.

Address for correspondence
(see Notes II, 1)

1. Demandeur

Les indications concernant le(s) demandeur(s) figurent dans la publication internationale ou ont été enregistrées par le Bureau international après la publication internationale.

Les changements qui n'ont pas encore été enregistrés par le Bureau international sont indiqués sur une feuille additionnelle.

Adresse pour la correspondance
(voir notice II, 1)

2. Vertreter

Name (Nur einen Vertreter angeben, der in das europäische Patentregister eingetragen und an den zugestellt wird)

Geschäftsanschrift

Telefon

Telefax

Telex



Weitere(r) Vertreter auf Zusatzblatt

2. Representative

Name (Name only one representative who will be listed in the Register of European Patents and to whom notification will be made)

Hutchins, Dr Michael Richard

Address of place of business

M. R. Hutchins & Co.
23 Mount Sion, Tunbridge Wells, Kent
TN1 1TZ, United Kingdom

Telephone

+44 1892 539659

Fax

+44 1892 528720

Additional representative(s) on additional sheet

2. Mandataire

Nom (N'indiquer qu'un seul mandataire, qui sera inscrit au Registre européen des brevets et auquel signification sera faite)

Adresse professionnelle

Téléphone

Téléfax

Telex

Autre(s) mandataire(s) sur une feuille additionnelle

3. Vollmacht



Einzelvollmacht ist beigelegt.



Allgemeine Vollmacht ist registriert unter Nummer:



Allgemeine Vollmacht ist eingereicht, aber noch nicht registriert.



Die beim EPA als PCT-Anmeldeamt eingereichte Vollmacht schließt ausdrücklich die europäische Phase ein.

3. Authorisation

Individual authorisation is attached.

General authorisation has been registered under No:

A general authorisation has been filed, but not yet registered.

The authorisation filed with the EPO as PCT receiving Office expressly includes the European phase.

3. Pouvoir

Un pouvoir spécial est joint.

Un pouvoir général a été enregistré sous le n° :

Un pouvoir général a été déposé, mais n'est pas encore enregistré.

Le pouvoir général déposé à l'OEB agissant en qualité d'office récepteur au titre du PCT s'applique expressément à la phase européenne.

<p><input checked="" type="checkbox"/> 4. Prüfungsantrag Hiermit wird die Prüfung der Anmeldung gemäß Art. 94 EPU beantragt. Die Prüfungsgebühr wird (wurde) entrichtet.</p> <p>Prüfungsantrag in einer zugelassenen Nichtamtssprache (siehe Merkblatt III, 5.2):</p>			<p>4. Request for examination Examination of the application under Art. 94 EPC is hereby requested. The examination fee is being (has been, will be) paid.</p> <p>Request for examination in an admissible non-EPO language (see Notes III, 5.2):</p>			<p>4. Requête en examen Il est demandé que soit examinée la demande de brevet conformément à l'art. 94 CBE. Il est (a été, sera) procédé au paiement de la taxe d'examen.</p> <p>Requête en examen dans une langue non officielle autorisée (voir notice III, 5.2):</p>		
<p><input checked="" type="checkbox"/> 5. Abschriften Zusätzliche Abschrift(en) der im ergänzenden europäischen Recherchenbericht angeführten Schriftstücke wird (werden) beantragt.</p> <p>Anzahl der zusätzlichen Sätze von Abschriften</p>			<p>5. Copies Additional copy (copies) of the documents cited in the supplementary European search report is (are) requested.</p> <p>Number of additional sets of copies</p>			<p>5. Copies Prière de fournir une ou plusieurs copies supplémentaires des documents cités dans le rapport complémentaire de recherche européenne.</p> <p>Nombre de jeux supplémentaires de copies</p>		
<p>6. Für das Verfahren vor dem EPA bestimmte Unterlagen</p> <p>6.1 Dem Verfahren vor dem EPA als Bestimmungsamt (PCT I) sind folgende Unterlagen zugrunde zu legen:</p> <p>die vom Internationalen Büro veröffentlichten Anmeldungsunterlagen (mit allen Ansprüchen, Beschreibung und Zeichnungen), gegebenenfalls mit den geänderten Ansprüchen nach Art. 19 PCT</p> <p><input checked="" type="checkbox"/> soweit sie nicht ersetzt werden durch die beigefügten Änderungen.</p> <p>Falls nötig, sind Klarstellungen auf einem Zusatzblatt einzureichen!</p>			<p>6. Documents intended for proceedings before the EPO</p> <p>6.1 Proceedings before the EPO as designated Office (PCT I) are to be based on the following documents:</p> <p>the application documents published by the International Bureau (with all claims, description and drawings), where applicable with amended claims under Art. 19 PCT</p> <p>unless replaced by the amendments enclosed.</p> <p>Where necessary, clarifications must be submitted on a separate sheet!</p>			<p>6. Pièces destinées à la procédure devant l'OEB</p> <p>6.1 La procédure devant l'OEB agissant en qualité d'office désigné (PCT I) doit se fonder sur les pièces suivantes :</p> <p>les pièces de la demande publiée par le Bureau international (avec toutes les revendications, la description et les dessins), éventuellement avec les revendications modifiées conformément à l'article 19 du PCT</p> <p>dans la mesure où elles ne sont pas remplacées par les modifications jointes.</p> <p>Le cas échéant, des explications doivent être jointes sur une feuille additionnelle!</p>		
<p>6.2 Dem Verfahren vor dem EPA als ausgewähltem Amt (PCT II) sind folgende Unterlagen zugrunde zu legen:</p> <p>die dem internationalen vorläufigen Prüfungsbericht zugrunde gelegten Unterlagen, einschließlich seiner eventuellen Anlagen (Solche Anlagen müssen immer beigefügt werden)</p> <p><input type="checkbox"/> soweit sie nicht ersetzt werden durch die beigefügten Änderungen.</p> <p>Falls nötig, sind Klarstellungen auf einem Zusatzblatt einzureichen!</p>			<p>6.2 Proceedings before the EPO as elected Office (PCT II) are to be based on the following documents:</p> <p>the documents on which the international preliminary examination report is based, including its possible annexes (Such annexes must always be filed)</p> <p>unless replaced by the amendments enclosed.</p> <p>Where necessary, clarifications must be submitted on a separate sheet!</p>			<p>6.2 La procédure devant l'OEB agissant en qualité d'office élu (PCT II) doit se fonder sur les pièces suivantes :</p> <p>les pièces sur lesquelles se fonde le rapport d'examen préliminaire international, y compris ses annexes éventuelles (De telles annexes sont toujours à joindre)</p> <p>dans la mesure où elles ne sont pas remplacées par les modifications jointes.</p> <p>Le cas échéant, des explications doivent être jointes sur une feuille additionnelle!</p>		
<p><input checked="" type="checkbox"/> Sind dem EPA als mit der internationalen vorläufigen Prüfung beauftragten Behörde Versuchsberichte zugegangen, dürfen diese dem Verfahren vor dem EPA zugrunde gelegt werden.</p>			<p>If the EPO as International Preliminary Examining Authority has received test reports, these may be used as the basis of proceedings before the EPO.</p>			<p>Si l'OEB, agissant en qualité d'administration chargée de l'examen préliminaire international, a reçu des rapports d'essais, ceux-ci peuvent constituer la base de la procédure devant l'OEB.</p>		

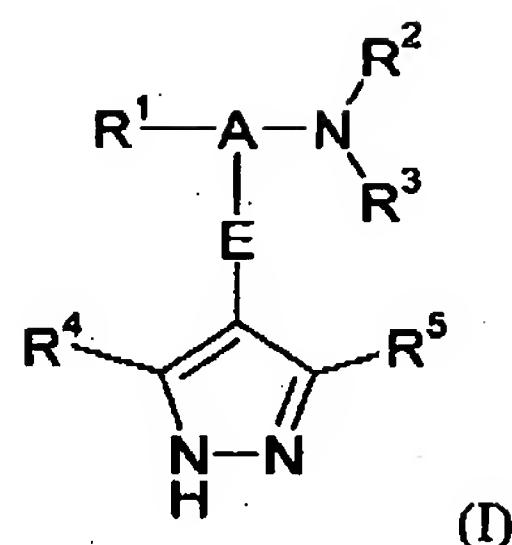
<p>7. Übersetzungen Beigefügt sind die nachfolgend angekreuzten Übersetzungen in einer der Amtssprachen des EPA (Deutsch, Englisch, Französisch):</p> <ul style="list-style-type: none"> <input type="checkbox"/> <i>Im Verfahren vor dem EPA als Bestimmungsamt oder ausgewähltem Amt (PCT I + II):</i> <input type="checkbox"/> Übersetzung der ursprünglich eingereichten internationalen Anmeldung (Beschreibung, Ansprüche, etwaige Textbestandteile in den Zeichnungen), der veröffentlichten Zusammenfassung, und etwaiger Angaben über biologisches Material nach Regel 13^{ab}.3 und 13^{ab}.4 PCT <input type="checkbox"/> Übersetzung der prioritätsbegründenden Anmeldung(en) <input type="checkbox"/> Es wird hiermit erklärt, daß die internationale Anmeldung in ihrer ursprünglich eingereichten Fassung eine vollständige Übersetzung der früheren Anmeldung ist (Regel 38(5) EPÜ) <input type="checkbox"/> <i>Zusätzlich im Verfahren vor dem EPA als Bestimmungsamt (PCT I):</i> <input type="checkbox"/> Übersetzung der nach Art. 19 PCT geänderten Ansprüche nebst Erklärung, falls diese dem Verfahren vor dem EPA zugrunde gelegt werden sollen (siehe Feld 6) <input type="checkbox"/> <i>Zusätzlich im Verfahren vor dem EPA als ausgewähltem Amt (PCT II):</i> <input type="checkbox"/> Übersetzung der Anlagen zum internationalen vorläufigen Prüfungsbericht 		
<p>7. Translations Translations in one of the official languages of the EPO (English, French, German) are enclosed as crossed below:</p> <ul style="list-style-type: none"> <i>In proceedings before the EPO as designated or elected Office (PCT I + II):</i> Translation of the international application (description, claims, any text in the drawings) as originally filed, of the abstract as published and of any indication under Rule 13^{ab}.3 and 13^{ab}.4 PCT regarding biological material Translation of the priority application(s) It is hereby declared that the international application as originally filed is a complete translation of the previous application (Rule 38(5) EPC) <i>In addition, in proceedings before the EPO as designated Office (PCT I):</i> Translation of amended claims and any statement under Art. 19 PCT, if the claims as amended are to form the basis for the proceedings before the EPO (see Section 6) <i>In addition, in proceedings before the EPO as elected Office (PCT II):</i> Translation of any annexes to the international preliminary examination report 		
<p>8. Biologisches Material Die Erfindung bezieht sich auf bzw. verwendet biologisches Material, das nach Regel 28 EPÜ hinterlegt worden ist.</p> <p><input type="checkbox"/> Die Angaben nach Regel 28(1)c) EPÜ (falls noch nicht bekannt, die Hinterlegungsstelle und das (die) Bezugszeichen [Nummer, Symbole usw.] des Hinterlegers) sind in der internationalen Veröffentlichung oder in der gemäß Feld 7 eingereichten Übersetzung enthalten auf:</p> <p>Seite(n) / Zeile(n)</p> <p><input type="checkbox"/> Die Empfangsbescheinigung(en) der Hinterlegungsstelle</p> <p><input type="checkbox"/> ist (sind) beigefügt</p> <p><input type="checkbox"/> wird (werden) nachgereicht</p> <p><input type="checkbox"/> Verzicht auf die Verpflichtung des Antragstellers nach Regel 28(3) EPÜ auf gesondertem Schriftstück</p>		
<p>8. Biological material The invention relates to and/or uses biological material deposited under Rule 28 EPC.</p> <p>The particulars referred to in Rule 28(1)(c) EPC (if not yet known, the depositary institution and the identification reference(s) (number, symbols etc.) of the depositor) are given in the international publication or in the translation submitted under Section 7 on:</p> <p>page(s) / line(s)</p> <p>The receipt(s) of deposit issued by the depositary institution</p> <p><input type="checkbox"/> is (are) enclosed</p> <p><input type="checkbox"/> will be filed at a later date</p> <p>Waiver of the right to an undertaking from the requester pursuant to Rule 28(3) EPC attached.</p>		
<p>8. Matière biologique L'invention concerne et/ou utilise de la matière biologique, déposée conformément à la règle 28 CBE.</p> <p>Les indications visées à la règle 28(1)c) CBE (si non encore connues, l'autorité de dépôt et la (les) référence(s) d'identification (numéro ou symboles etc.) du déposant) figurent dans la publication internationale ou dans une traduction produite conformément à la rubrique 7 à la / aux:</p> <p>page(s) / ligne(s)</p> <p>Le(s) récépissé(s) de dépôt délivré(s) par l'autorité de dépôt</p> <p><input type="checkbox"/> est (sont) joint(s)</p> <p><input type="checkbox"/> sera (seront) produit(s) ultérieurement</p> <p>Renonciation, sur document distinct, à l'engagement du requérant au titre de la règle 28(3) CBE.</p>		

<p>9. Nucleotid- und Aminosäure-Sequenzen</p> <p><input type="checkbox"/> Die nach Regeln 5.2 und 13^{er} PCT sowie Regel 111(3) EPÜ erforderlichen Unterlagen liegen dem EPA bereits vor.</p> <p><input type="checkbox"/> Das schriftliche Sequenzprotokoll wird anliegend nachgereicht.</p> <p><input type="checkbox"/> Das Sequenzprotokoll geht nicht über den Inhalt der Anmeldung in der ursprünglich eingereichten Fassung hinaus.</p> <p><input type="checkbox"/> Der vorgeschriebene Datenträger ist beigefügt.</p> <p><input type="checkbox"/> Die auf dem Datenträger gespeicherte Information stimmt mit dem schriftlichen Sequenzprotokoll überein.</p>			<p>9. Nucleotide and amino acid sequences</p> <p>The items necessary in accordance with Rules 5.2 and 13^{er} PCT and Rule 111(3) EPC have already been furnished to the EPO.</p> <p>The written sequence listing is furnished herewith.</p> <p>The sequence listing does not include matter which goes beyond the content of the application as filed.</p> <p>The prescribed data carrier is enclosed.</p> <p>The information recorded on the data carrier is identical to the written sequence listing.</p>			<p>9. Séquences de nucléotides et d'acides aminés</p> <p>Les pièces requises selon les règles 5.2 et 13^{er} PCT et la règle 111(3) CBE ont déjà été déposées auprès de l'OEB.</p> <p>La liste de séquences écrite est produite ci-joint.</p> <p>La liste de séquences ne contient pas d'éléments s'étendant au-delà du contenu de la demande telle qu'elle a été déposée.</p> <p>Le support de données prescrit est joint.</p> <p>L'information figurant sur le support de données est identique à celle que contient la liste de séquences écrite.</p>		
<p>10. Benennungsgebühren</p> <p><input checked="" type="checkbox"/> 10.1 Es ist derzeit beabsichtigt, den siebenfachen Betrag einer Benennungsgebühr zu entrichten. Damit gelten die Benennungsgebühren für alle Vertragsstaaten des EPÜ¹ als entrichtet (Art. 2 Nr. 3 GebO), soweit sie in der internationalen Anmeldung bestimmt sind².</p> <p><input type="checkbox"/> 10.2 Abweichend von der Erklärung in Nr. 10.1 ist derzeit beabsichtigt, weniger als sieben Benennungsgebühren für folgende in der internationalen Anmeldung bestimmte Vertragsstaaten des EPÜ² zu entrichten:</p> <p>(1) <input type="checkbox"/> _____</p> <p>(2) <input type="checkbox"/> _____</p> <p>(3) <input type="checkbox"/> _____</p>			<p>10. Designation fees</p> <p>10.1 It is currently intended to pay seven times the amount of the designation fee. The designation fees for all the EPC contracting states¹ designated in the international application² are thereby deemed to have been paid (Art. 2 No. 3 RFEes).</p> <p>10.2 The declaration in No. 10.1 does not apply. Instead, it is currently intended to pay fewer than seven designation fees for the following EPC contracting states² designated in the international application:</p> <p>(4) <input type="checkbox"/> _____</p> <p>(5) <input type="checkbox"/> _____</p> <p>(6) <input type="checkbox"/> _____</p>			<p>10. Taxes de désignation</p> <p>10.1 Il est actuellement envisagé de payer un montant correspondant à sept fois la taxe de désignation. Les taxes de désignation sont ainsi réputées payées pour tous les Etats contractants de la CBE¹ désignés dans la demande internationale² (art. 2, point 3 du RRT).</p> <p>10.2 Contrairement à ce qui est indiqué au n° 10.1, il est actuellement envisagé de payer moins de sept taxes de désignation pour les Etats contractants de la CBE² suivants désignés dans la demande internationale :</p> <p>(4) <input type="checkbox"/> _____</p> <p>(5) <input type="checkbox"/> _____</p> <p>(6) <input type="checkbox"/> _____</p>		
<p>Soweit unter Nr. 10.2 Vertragsstaaten aufgeführt sind, wird beantragt, für die dort nicht aufgeführten Vertragsstaaten von der Zustellung einer Mitteilung nach Regel 108(3) EPÜ abzusehen.</p> <p><input checked="" type="checkbox"/> 10.3 Wird ein automatischer Abbuchungsauftrag erteilt (Feld 12), so wird das EPA beauftragt, bei Ablauf der Grundfrist nach Regel 107 (1)d) EPÜ den siebenfachen Betrag einer Benennungsgebühr abzubuchen. Ist eine Erklärung nach Nr. 10.2 abgegeben worden, so sollen die Benennungsgebühren nur für die dort angegebenen Vertragsstaaten abgebucht werden, sofern dem EPA nicht bis zum Ablauf der Grundfrist ein anderslautender Auftrag zugeht.</p>			<p>If contracting states are indicated under No. 10.2, it is requested that no communication under Rule 108(3) EPC be issued for contracting states not thus indicated.</p> <p>10.3 If an automatic debit order has been issued (Section 12), the EPO is authorised, on expiry of the basic period under Rule 107(1)(d) EPC, to debit seven times the amount of the designation fee. If states are indicated under No. 10.2, the EPO will debit designation fees only for those states, unless instructed otherwise before the basic period expires.</p>			<p>Si des Etats contractants sont mentionnés au n° 10.2, prière de ne pas procéder à la signification d'une notification prévue par la règle 108(3) CBE pour les Etats contractants n'y étant pas mentionnés.</p> <p>10.3 Si un ordre de prélèvement automatique est donné (rubrique 12), il est demandé à l'OEB de prélever, à l'expiration du délai normal visé à la règle 107(1)d) CBE, un montant correspondant à sept fois la taxe de désignation. Si une déclaration a été faite au n° 10.2, les taxes de désignation ne sont à prélever que pour les Etats contractants qui y sont indiqués, sauf instruction contraire reçue par l'OEB avant l'expiration du délai normal.</p>		
<p><small>1 Stand bei Drucklegung: 27 Vertragsstaaten, und zwar: / Status when this form was printed: 27 contracting states, namely / Situation à la date d'impression : 27 Etats contractants, à savoir : AT Österreich / Austria / Autriche, BE Belgien / Belgium / Belgique, BG Bulgarien / Bulgaria / Bulgarie, CH / LI Schweiz und Liechtenstein / Switzerland and Liechtenstein / Suisse et Liechtenstein, CY Zypern / Cyprus / Chypre, CZ Tschechische Republik / Czech Republic / République tchèque, DE Deutschland / Germany / Allemagne, DK Danemark / Danemark / Danimarca, EE Estland / Estonia / Estonie, ES Spanien / Spain / Espagne, FI Finnland / Finland / Finlande, FR Frankreich / France / France, GB Vereinigtes Königreich / United Kingdom / Royaume-Uni, GR Griechenland / Greece / Grèce, HU Ungarn / Hungary / Hongrie, IE Irland / Ireland / Irlande, IT Italien / Italy / Italie, LU Luxemburg / Luxembourg / Luxembourg, MC Monaco / Monaco / Monaco, NL Niederlande / Netherlands / Pays-Bas, PT Portugal / Portugal / Portugal, RO Rumänien / Romania / Roumanie, SE Schweden / Sweden / Suède, SI Slowenien / Slovenia / Slovénie, SK Slowakische Republik / Slovak Republic / République slovaque, TR Türkei / Turkey / Turquie</small></p> <p><small>2 Für folgende Staaten nur möglich, falls in der internationalen Anmeldung am oder nach folgendem Tag bestimmt: Slowakische Republik, Bulgarien, Tschechische Republik und Estland: 1. Juli 2002, Slowenien: 1. Dezember 2002, Ungarn: 1. Januar 2003 und Rumänien: 1. März 2003. / For the following states this is possible only if they are designated in the international application on or after the stated date: Slovak Republic, Bulgaria, Czech Republic and Estonia: 1 July 2002, Slovenia: 1 December 2002, Hungary: 1 January 2003 and Romania: 1 March 2003. / En ce qui concerne les Etats suivants seulement si la désignation a été effectuée dans la demande internationale à la date suivante ou à une date ultérieure: République slovaque, Bulgarie, République tchèque et Estonie: 1^{er} juillet 2002, Slovénie: 1^{er} décembre 2002, Hongrie: 1^{er} janvier 2003 et Roumanie: 1^{er} mars 2003.</small></p>								

<p><input checked="" type="checkbox"/> 11. Erstreckung des europäischen Patents Bei Zahlung der Erstreckungsgebühr(en) gilt diese Anmeldung auch als wirksamer Erstreckungsantrag für die in der internationalen Anmeldung bestimmten »Erstreckungsstaaten«. Es ist beabsichtigt, diese Gebühr(en) für folgende Staaten zu entrichten:</p> <table> <tr> <td><input type="checkbox"/></td> <td>SI</td> <td>Slowenien¹⁾</td> <td><input type="checkbox"/></td> <td>Slovenia¹⁾</td> <td>Lithuania</td> <td><input type="checkbox"/></td> <td>Slovénie¹⁾</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>LT</td> <td>Litauen</td> <td><input type="checkbox"/></td> <td>Latvia</td> <td>Lettonie</td> <td><input type="checkbox"/></td> <td>Lituanie</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>LV</td> <td>Lettland</td> <td><input type="checkbox"/></td> <td>Albania</td> <td>Albanie</td> <td><input type="checkbox"/></td> <td>Albanie</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>AL</td> <td>Albanien</td> <td><input type="checkbox"/></td> <td>Romania¹⁾</td> <td>Roumanie¹⁾</td> <td><input type="checkbox"/></td> <td>Roumanie¹⁾</td> </tr> <tr> <td><input type="checkbox"/></td> <td>RO</td> <td>Rumänien¹⁾</td> <td><input type="checkbox"/></td> <td>Former Yugoslav Republic of Macedonia</td> <td>Ex-République yougoslave de Macédoine</td> <td><input type="checkbox"/></td> <td>Ex-République yougoslave de Macédoine</td> </tr> <tr> <td><input type="checkbox"/></td> <td>MK</td> <td>Ehemalige jugoslawische Republik Mazedonien</td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </table>			<input type="checkbox"/>	SI	Slowenien ¹⁾	<input type="checkbox"/>	Slovenia ¹⁾	Lithuania	<input type="checkbox"/>	Slovénie ¹⁾	<input checked="" type="checkbox"/>	LT	Litauen	<input type="checkbox"/>	Latvia	Lettonie	<input type="checkbox"/>	Lituanie	<input checked="" type="checkbox"/>	LV	Lettland	<input type="checkbox"/>	Albania	Albanie	<input type="checkbox"/>	Albanie	<input checked="" type="checkbox"/>	AL	Albanien	<input type="checkbox"/>	Romania ¹⁾	Roumanie ¹⁾	<input type="checkbox"/>	Roumanie ¹⁾	<input type="checkbox"/>	RO	Rumänien ¹⁾	<input type="checkbox"/>	Former Yugoslav Republic of Macedonia	Ex-République yougoslave de Macédoine	<input type="checkbox"/>	Ex-République yougoslave de Macédoine	<input type="checkbox"/>	MK	Ehemalige jugoslawische Republik Mazedonien					
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<input type="checkbox"/>	MK	Ehemalige jugoslawische Republik Mazedonien																																																
<p>1) Für Slowenien und Rumänien nur möglich, falls in der internationalen Anmeldung bis 30. November 2002 (Slowenien) oder bis 28. Februar 2003 (Rumänien) bestimmt. / For Slovenia and Romania this is possible only if they are designated in the international application up to 30 November 2002 (Slovenia) or 28 February 2003 (Romania). / En ce qui concerne la Slovénie et la Roumanie, seulement si la désignation a été effectuée dans la demande internationale jusqu'au 30 novembre 2002 (Slovénie) ou jusqu'au 28 février 2003 (Roumanie).</p> <p>2) Platz für Staaten, mit denen »Erstreckungsabkommen« nach Drucklegung dieses Formblatts in Kraft treten und die in der internationalen Anmeldung bestimmt waren. / Space for States with which «extension agreements» enter into force after this form has been printed and which were designated in the international application. / Prévu pour des Etats à l'égard desquels des «accords d'extension» entrenteront en vigueur après l'impression du présent formulaire et qui ont été désignés dans la demande internationale.</p>																																																		
<p>12. Automatischer Abbuchungsauftrag (Nur möglich für Inhaber von beim EPA geführten laufenden Konten) Das EPA wird beauftragt, nach Maßgabe der Vorschriften über das automatische Abbuchungsverfahren fällige Gebühren und Auslagen vom untenstehenden laufenden Konto abzubuchen. In Bezug auf die Benennungsgebühren wird auf Feld 10.3 verwiesen. Das EPA wird ferner beauftragt, die Erstreckungsgebühren für jeden in Feld 11 angekreuzten »Erstreckungsstaat« bei Ablauf der Grundfrist zu ihrer Zahlung abzubuchen, sofern ihm nicht bis dahin ein anderslautender Auftrag zugeht.</p> <p>Nummer und Kontoinhaber</p>																																																		
<p>12. Automatic debit order (for EPO deposit account holders only) The EPO is hereby authorised, under the Arrangements for the automatic debiting procedure, to debit from the deposit account below any fees and costs falling due. For designation fees, see Section 10.3. The EPO is also authorised, on expiry of the basic period for paying the extension fees, to debit those fees for each of the «extension states» marked with a cross in Section 11, unless instructed otherwise before the said period expires.</p> <p>Number and account holder</p> <p>28050421 M. R. Hutchins & Co.</p>																																																		
<p>13. Eventuelle Rückzahlungen auf das beim EPA geführte laufende Konto Nummer und Kontoinhaber</p>																																																		
<p>13. Any reimbursement to EPO deposit account Number and account holder</p> <p>28050421 M. R. Hutchins & Co.</p>																																																		
<p>14. Unterschrift(en) des (der) Anmelder(s) oder Vertreters</p> <p>Ort / Datum</p> <p>Für Angestellte (Art. 133(3) EPÖ) mit allgemeiner Vollmacht:</p> <p>Nr.</p> <p>Name(n) des (der) Unterzeichneten bitte in Druckschrift wiederholen. Bei juristischen Personen bitte auch die Stellung des (der) Unterzeichneten innerhalb der Gesellschaft in Druckschrift angeben.</p>																																																		
<p>14. Signature(s) of applicant(s) or representative Dr Michael R. Hutchins</p> <p>Place / Date Tunbridge Wells 23.7.2006</p> <p>For employees (Art. 133(3) EPC) having a general authorisation:</p> <p>No.</p> <p>Please print name(s) under signature(s). In the case of legal persons, the position of the signatory within the company should also be printed.</p>																																																		
<p>14. Signature(s) du (des) demandeur(s) ou du mandataire</p> <p>Lieu / Date</p> <p>Pour les employés (art. 133(3) CBE) disposant d'un pouvoir général :</p> <p>N°</p> <p>Le ou les noms des signataires doivent être indiqués en caractères d'imprimerie. S'il s'agit d'une personne morale, la position occupée au sein de celle-ci par le ou les signataire(s) doit également être indiquée en caractères d'imprimerie.</p>																																																		

CLAIMS

1. A compound of the formula (I):



or a salt, solvate, tautomer or N-oxide thereof;

5 wherein A is a saturated hydrocarbon linker group containing from 1 to 7 carbon atoms, the linker group having a maximum chain length of 5 atoms extending between R¹ and NR²R³ and a maximum chain length of 4 atoms extending between E and NR²R³, wherein one of the carbon atoms in the linker group may optionally be replaced by an oxygen or nitrogen atom; and wherein the carbon atoms of the linker group A may optionally bear one or more substituents selected from oxo, fluorine and hydroxy, provided that the hydroxy group when present is not located at a carbon atom α with respect to the NR²R³ group and provided that the oxo group when present is located at a carbon atom α with respect to the NR²R³ group;

10 E is a monocyclic or bicyclic carbocyclic or heterocyclic group;

15 R¹ is an aryl or heteroaryl group;

20 R² and R³ are independently selected from hydrogen, C₁₋₄ hydrocarbyl and C₁₋₄ acyl wherein the hydrocarbyl and acyl moieties are optionally substituted by one or more substituents selected from fluorine, hydroxy, amino, methylamino, dimethylamino and methoxy;

25 or R² and R³ together with the nitrogen atom to which they are attached form a cyclic group selected from an imidazole group and a saturated monocyclic

heterocyclic group having 4-7 ring members and optionally containing a second heteroatom ring member selected from O and N;

5 or one of R² and R³ together with the nitrogen atom to which they are attached and one or more atoms from the linker group A form a saturated monocyclic heterocyclic group having 4-7 ring members and optionally containing a second heteroatom ring member selected from O and N;

10 or NR²R³ and the carbon atom of linker group A to which it is attached together form a cyano group;

15 R⁴ is selected from hydrogen, halogen, C₁₋₅ saturated hydrocarbyl, C₁₋₅ saturated hydrocarbyloxy, cyano, and CF₃; and

20 R⁵ is selected from hydrogen, halogen, C₁₋₅ saturated hydrocarbyl, C₁₋₅ saturated hydrocarbyloxy, cyano, CONH₂, CONHR⁹, CF₃, NH₂, NHCOR⁹ or NHCONHR⁹;

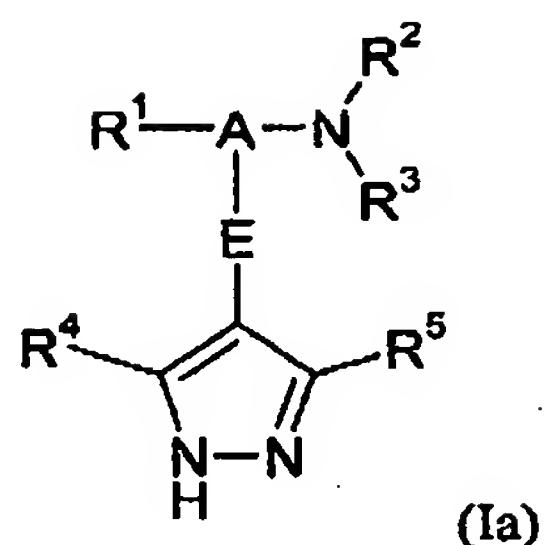
25 R⁹ is a group R^{9a} or (CH₂)R^{9a}, wherein R^{9a} is a monocyclic or bicyclic group which may be carbocyclic or heterocyclic;

the carbocyclic group or heterocyclic group R^{9a} being optionally substituted by one or more substituents selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, mono- or di-C₁₋₄ hydrocarbylamino; a group R^a-R^b wherein R^a is a bond, O, CO, X¹C(X²), C(X²)X¹, X¹C(X²)X¹, S, SO, SO₂, NR^c, SO₂NR^c or NR^cSO₂; and R^b is selected from hydrogen, heterocyclic groups having from 3 to 12 ring members, and a C₁₋₈ hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di-C₁₋₄ hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the C₁₋₈ hydrocarbyl group may optionally be replaced by O, S, SO, SO₂, NR^c, X¹C(X²), C(X²)X¹ or X¹C(X²)X¹;

30 R^c is selected from hydrogen and C₁₋₄ hydrocarbyl; and

X¹ is O, S or NR^c and X² is =O, =S or =NR^c.

30 2. A compound according to claim 1 of the formula (Ia):



or a salt, solvate, tautomer or N-oxide thereof;
wherein A is a saturated hydrocarbon linker group containing from 1 to 7 carbon atoms, the linker group having a maximum chain length of 5 atoms extending between R¹ and NR²R³ and a maximum chain length of 4 atoms extending between E and NR²R³, wherein one of the carbon atoms in the linker group may optionally be replaced by an oxygen or nitrogen atom; and wherein the carbon atoms of the linker group A may optionally bear one or more substituents selected from oxo, fluorine and hydroxy, provided that the hydroxy group when present is not located at a carbon atom α with respect to the NR²R³ group and provided that the oxo group when present is located at a carbon atom α with respect to the NR²R³ group;
E is a monocyclic or bicyclic carbocyclic or heterocyclic group;
R¹ is an aryl or heteroaryl group;
R² and R³ are independently selected from hydrogen, C₁₋₄ hydrocarbyl and C₁₋₄ acyl;
or R² and R³ together with the nitrogen atom to which they are attached form a saturated monocyclic heterocyclic group having 4-7 ring members and optionally containing a second heteroatom ring member selected from O and N;
or one of R² and R³ together with the nitrogen atom to which they are attached and one or more atoms from the linker group A form a saturated monocyclic heterocyclic group having 4-7 ring members and optionally containing a second heteroatom ring member selected from O and N;

or NR^2R^3 and the carbon atom of linker group A to which it is attached together form a cyano group;

R^4 is selected from hydrogen, halogen, C_{1-5} saturated hydrocarbyl, cyano and CF_3 ; and

5 R^5 is selected from hydrogen, halogen, C_{1-5} saturated hydrocarbyl, cyano, $CONH_2$, $CONHR^9$, CF_3 , NH_2 , $NHCOR^9$ or $NHCONHR^9$;

10 R^9 is phenyl or benzyl each optionally substituted by one or more substituents selected from halogen, hydroxy, trifluoromethyl, cyano, nitro, carboxy, amino, mono- or di- C_{1-4} hydrocarbylamino; a group R^a-R^b wherein R^a is a bond, O, CO, $X^1C(X^2)$, $C(X^2)X^1$, $X^1C(X^2)X^1$, S, SO, SO_2 , NR^c , SO_2NR^c or NR^cSO_2 ; and R^b is selected from hydrogen, heterocyclic groups having from 3 to 12 ring members, and a C_{1-8} hydrocarbyl group optionally substituted by one or more substituents selected from hydroxy, oxo, halogen, cyano, nitro, carboxy, amino, mono- or di- C_{1-4} hydrocarbylamino, carbocyclic and heterocyclic groups having from 3 to 12 ring members and wherein one or more carbon atoms of the C_{1-8} hydrocarbyl group may optionally be replaced by O, S, SO, SO_2 , NR^c , $X^1C(X^2)$, $C(X^2)X^1$ or $X^1C(X^2)X^1$;

15 R^c is selected from hydrogen and C_{1-4} hydrocarbyl; and

X^1 is O, S or NR^c and X^2 is =O, =S or = NR^c .

20 3. A compound according to claim 1 or claim 2 wherein A is a saturated hydrocarbon linker group containing from 1 to 7 carbon atoms, the linker group having a maximum chain length of 5 atoms extending between R^1 and NR^2R^3 and a maximum chain length of 4 atoms extending between E and NR^2R^3 , wherein one of the carbon atoms in the linker group may optionally be replaced by an oxygen or nitrogen atom; and wherein the carbon atoms of the linker group A may optionally bear one or more substituents selected from fluorine and hydroxy, provided that the hydroxy group when present is not located at a carbon atom α with respect to the NR^2R^3 group; and

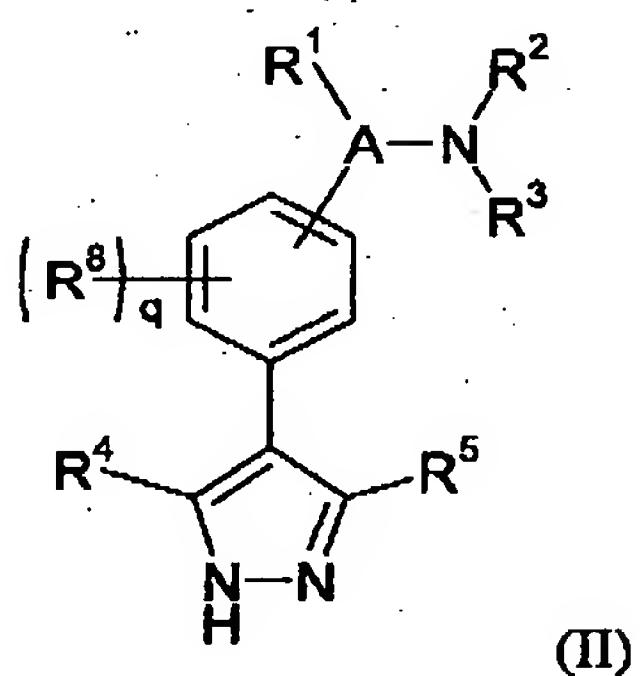
25 R^5 is selected from selected from hydrogen, halogen, C_{1-5} saturated hydrocarbyl, cyano, $CONH_2$, CF_3 , NH_2 , $NHCOR^9$ and $NHCONHR^9$.

4. A compound according to any one of claims 1 to 3 wherein:
 - (i) the linker group A has a maximum chain length of 3 atoms (more preferably 1 or 2 atoms, and most preferably 2 atoms) extending between R^1 and NR^2R^3 ; and/or
 - 5 (ii) the linker group A has a maximum chain length of 3 atoms extending between E and NR^2R^3 ; and/or
 - (iii) the linker group A has a chain length of 2 or 3 atoms extending between R^1 and NR^2R^3 and a chain length of 2 or 3 atoms extending between E and NR^2R^3 ; and/or
 - 10 (iv) the linker group atom linked directly to the group E is a carbon atom and the linker group A has an all-carbon skeleton.
5. A compound according to any one of claims 1 to 3 wherein the portion R^1 -A- NR^2R^3 of the compound is represented by the formula R^1 -(G)_k-(CH₂)_m-W-O_b-(CH₂)_n-(CR⁶R⁷)_p-NR²R³ wherein G is NH, NMe or O; W is attached to the group E and is selected from (CH₂)_j-CR²⁰, (CH₂)_j-N and (NH)_j-CH; b is 0 or 1, j is 0 or 1, k is 0 or 1, m is 0 or 1, n is 0, 1, 2, or 3 and p is 0 or 1; the sum of b and k is 0 or 1; the sum of j, k, m, n and p does not exceed 4; R⁶ and R⁷ are the same or different and are selected from methyl and ethyl, or CR⁶R⁷ forms a cyclopropyl group; and R²⁰ is selected from hydrogen, methyl, hydroxy and fluorine.
- 15 20 6. A compound according to any one of claims 1 to 3 wherein the moiety R^1 -A- NR^2R^3 is represented by the formula R^1 -(G)_k-(CH₂)_m-X-(CH₂)_n-(CR⁶R⁷)_p-NR²R³ wherein G is NH, NMe or O; X is attached to the group E and is selected from (CH₂)_j-CH, (CH₂)_j-N and (NH)_j-CH; j is 0 or 1, k is 0 or 1, m is 0 or 1, n is 0, 1, 2, or 3 and p is 0 or 1, and the sum of j, k, m, n and p does not exceed 4; and R⁶ and R⁷ are the same or different and are selected from methyl and ethyl, or CR⁶R⁷ forms a cyclopropyl group.

7. A compound according to claim 6 wherein (i) k is 0, m is 0 or 1, n is 0, 1, 2 or 3 and p is 0; or (ii) k is 0, m is 0 or 1, n is 0, 1 or 2 and p is 1.
8. A compound according to claim 6 wherein (i) X is $(CH_2)_j\text{-CH}$, k is 1, m is 0, n is 0, 1, 2 or 3 and p is 0; or (ii) X is $(CH_2)_j\text{-CH}$, k is 1, m is 0, n is 0, 1 or 2 and p is 1.
- 5 9. A compound according to claim 6 or claim 8 wherein (i) j is 0; or (ii) j is 1; or (iii) CR^6R^7 is $C(CH_3)_2$.
10. A compound according to claim 6 wherein the portion $R^1\text{-A-NR}^2R^3$ of the compound is represented by the formula $R^1\text{-X-}(CH_2)_n\text{-NR}^2R^3$ where X is attached to the group E and is a group CH, and n is 2.
- 10 11. A compound according to claim 1 or claim 2 wherein $R^1\text{-A(E)-NR}^2R^3$ is (i) a group selected from the groups A1 to A11 set out in Table 1 herein; or (ii) is selected from groups A1, A2, A3 and A10 in Table 1; or (iii) is the group A10 in Table 1.
12. A compound according to any one of the preceding claims wherein:
 - 15 (a) E is an aryl or heteroaryl group such as optionally substituted phenyl, thiophene, furan, pyrimidine and pyridine groups; or
 - (b) E is a phenyl group; or
 - (c) E is a non-aromatic monocyclic group selected from cycloalkanes such as cyclohexane and cyclopentane, and nitrogen-containing rings such as piperazine
- 20 (d) E is a monocyclic group.
13. A compound according to any one of the preceding claims wherein the group A and the pyrazole group are attached to the group E in a *meta* or *para* relative orientation; i.e. A and the pyrazole group are not attached to adjacent ring members of the group E, for example wherein E is selected from 1,4-phenylene, 1,3-phenylene, 2,5-pyridylene and 2,4-pyridylene, 1,4-piperazinyl, and 1,4-piperazonyl.

14. A compound according to any one of the preceding claims wherein E is (i) unsubstituted or (ii) has up to 4 substituents (e.g. 0-3 substituents, more preferably 0-2 substituents, for example 0 or 1 substituent) R⁸ selected from hydroxy, oxo (when E is non-aromatic), chlorine, bromine, trifluoromethyl, cyano, C₁₋₄ hydrocarbyloxy and C₁₋₄ hydrocarbyl optionally substituted by C₁₋₂ alkoxy or hydroxy.

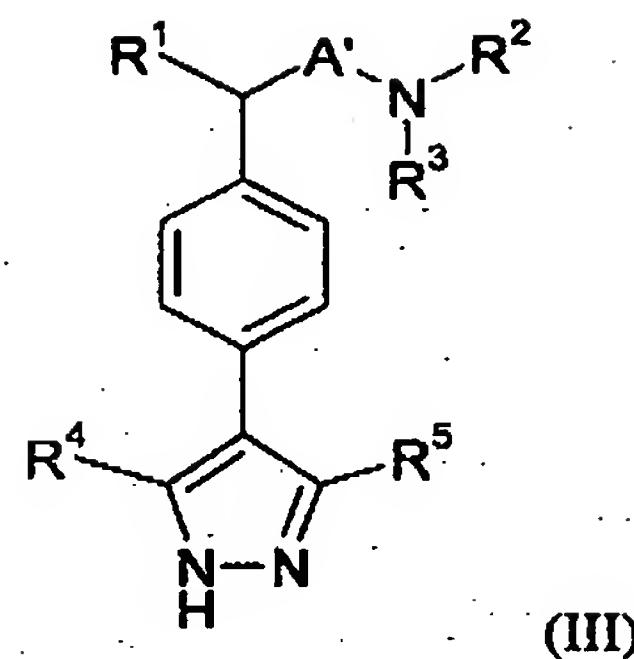
5 15. A compound according to claim 12 having the formula (II):



10 wherein the group A is attached to the *meta* or *para* position of the benzene ring and q is 0-4 (for example wherein q is 0, 1 or 2, preferably 0 or 1 and most preferably 0); R⁸ is hydroxy; halogen (e.g. chlorine and bromine); trifluoromethyl; cyano; C₁₋₄ hydrocarbyloxy optionally substituted by C₁₋₂ alkoxy or hydroxy; and C₁₋₄ hydrocarbyl optionally substituted by C₁₋₂ alkoxy or hydroxy.

16. A compound according to claim 13 having the formula (III):

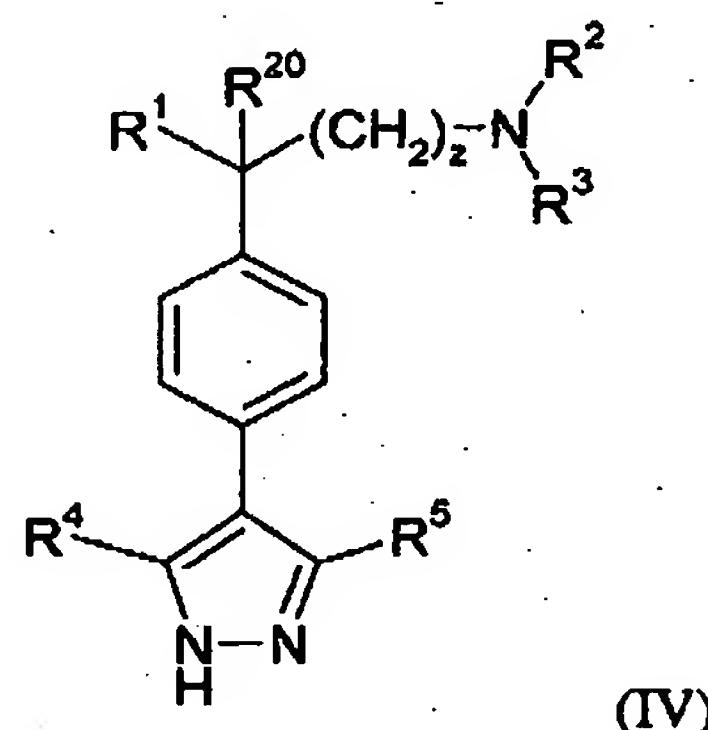
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(III)

where A' is the residue of the group A and R^1 to R^5 are as defined in any one of the preceding claims.

17. A compound according to claim 15 having the formula (IV):

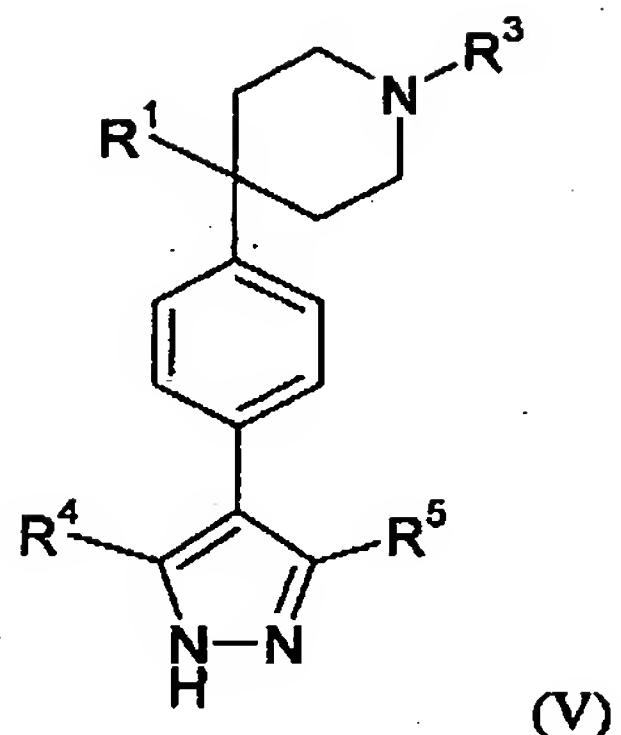


(IV)

5

wherein z is 0, 1 or 2, R^{20} is selected from hydrogen, methyl, hydroxy and fluorine, provided that when z is 0, R^{20} is other than hydroxy.

18. A compound according to claim 15 having the formula (V):



wherein R³ is optionally selected from hydrogen and C₁₋₄ hydrocarbyl, for example C₁₋₄ alkyl such as methyl, ethyl and isopropyl, and more preferably R³ is hydrogen.

5 19. A compound according to any one of the preceding claims wherein R¹ is selected from phenyl, naphthyl, thienyl, furan, pyrimidine and pyridine, and preferably wherein R¹ is phenyl.

20. A compound according to any one of the preceding claims wherein R¹ is unsubstituted or bears one or more substituents selected from hydroxy; C₁₋₄ acyloxy; fluorine; chlorine; bromine; trifluoromethyl; cyano; CONH₂; nitro; C₁₋₄ hydrocarbyloxy and C₁₋₄ hydrocarbyl each optionally substituted by C₁₋₂ alkoxy, carboxy or hydroxy; C₁₋₄ acylamino; benzoylamino; pyrrolidinocarbonyl; piperidinocarbonyl; morpholinocarbonyl; piperazinocarbonyl; five and six membered heteroaryl and heteroaryloxy groups containing one or two heteroatoms selected from N, O and S; phenyl; phenyl-C₁₋₄ alkyl; phenyl-C₁₋₄ alkoxy; heteroaryl-C₁₋₄ alkyl; heteroaryl-C₁₋₄ alkoxy and phenoxy, wherein the heteroaryl, heteroaryloxy, phenyl, phenyl-C₁₋₄ alkyl, phenyl-C₁₋₄ alkoxy, heteroaryl-C₁₋₄ alkyl, heteroaryl-C₁₋₄ alkoxy and phenoxy groups are each optionally substituted with 1, 2 or 3 substituents selected from C₁₋₂ acyloxy, fluorine, chlorine, bromine, trifluoromethyl, cyano, CONH₂, C₁₋₂ hydrocarbyloxy and C₁₋₂ hydrocarbyl each optionally substituted by methoxy or hydroxy.

21. A compound according to claim 20 wherein:
 - (a) R¹ is unsubstituted or is substituted by up to 5 substituents (e.g. 0, 1, 2, 3 or 4 substituents, preferably 0, 1, 2 or 3, and more preferably 0, 1 or 2 substituents) selected from hydroxy; C₁₋₄ acyloxy; fluorine; chlorine; bromine; trifluoromethyl; 5 cyano; C₁₋₄ hydrocarbyloxy and C₁₋₄ hydrocarbyl optionally substituted by C₁₋₂ alkoxy or hydroxy; and five membered heteroaryl groups containing one or two heteroatoms selected from N, O and S, the heteroaryl groups being optionally substituted by one or more C₁₋₄ alkyl substituents; or
 - (b) R¹ is unsubstituted or is substituted by up to 5 substituents (e.g. 0, 1, 2, 3 or 4 substituents, preferably 0, 1, 2 or 3, and more preferably 0, 1 or 2 substituents) selected from hydroxy, C₁₋₄ acyloxy, fluorine, chlorine, bromine, trifluoromethyl, 10 cyano, C₁₋₄ hydrocarbyloxy and C₁₋₄ hydrocarbyl optionally substituted by C₁₋₂ alkoxy or hydroxy.
22. A compound according to claim 21 wherein the group R¹ has one or two 15 substituents selected from fluorine, chlorine, trifluoromethyl, methyl and methoxy.
23. A compound according to claim 22 wherein R¹ is a mono-chlorophenyl or dichlorophenyl group.
24. A compound according to any one of the preceding claims wherein (a) R⁴ is 20 selected from hydrogen and methyl; and/or (b) R⁵ is selected from hydrogen, fluorine, chlorine, bromine, methyl, ethyl, hydroxyethyl, methoxymethyl, cyano, CF₃, NH₂, NHCOR^{9b} and NHCONHR^{9b} where R^{9b} is phenyl or benzyl optionally substituted by hydroxy, C₁₋₄ acyloxy, fluorine, chlorine, bromine, trifluoromethyl, cyano, C₁₋₄ hydrocarbyloxy and C₁₋₄ hydrocarbyl optionally substituted by C₁₋₂ 25 alkoxy or hydroxy.
25. A compound according to any one of the preceding claims wherein:

(a) R^2 and R^3 are independently selected from hydrogen, C_{1-4} hydrocarbyl and C_{1-4} acyl; or

(b) R^2 and R^3 are independently selected from hydrogen and methyl; or

(c) R^2 and R^3 are both hydrogen.

5 26. A compound according to any one of the preceding claims having a molecular weight no greater than 1000, more usually less than 750, for example less than 700, or less than 650, or less than 600, or less than 550, or less than 525, for example 500 or less.

27. A compound of the formula (I) which is:

10 2-phenyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;
3-phenyl-2-[3-(1H-pyrazol-4-yl)-phenyl]-propionitrile;
2-[4-(3,5-dimethyl-1H-pyrazol-4-yl)-phenyl]-2-phenyl-ethylamine;
2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;
2-[3-(3,5-dimethyl-1H-pyrazol-4-yl)-phenyl]-1-phenyl-ethylamine;

15 3-phenyl-2-[3-(1H-pyrazol-4-yl)-phenyl]-propylamine;
3-phenyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;
{3-(4-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;
{3-(3,4-difluoro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;
{3-(3-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;

20 3-(4-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propionamide;
3-(4-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;
3-(3,4-dichloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;
4-(4-chloro-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;
4-(4-methoxy-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;

25 4-(4-chloro-phenyl)-1-methyl-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;
4-phenyl-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;
4-[4-(3,5-dimethyl-1H-pyrazol-4-yl)-phenyl]-4-phenyl-piperidine;
dimethyl-{3-[4-(1H-pyrazol-4-yl)-phenyl]-3-pyridin-2-yl-propyl}-amine;
{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-dimethyl-amine;

{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine (R);
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine (S);
 4-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-morpholine;

5 4-{4-[1-(4-chloro-phenyl)-2-pyrrolidin-1-yl-ethyl]-phenyl}-1H-pyrazole;
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-isopropyl-amine;
 dimethyl-{2-phenyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-amine;
 {2,2-bis-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-dimethyl-amine;
 {2,2-bis-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;

10 2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine (R);
 2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine (S);
 2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-acetamide;
 1-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-piperazine;
 1-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-piperidine;

15 4-{4-[2-azetidin-1-yl-1-(4-chloro-phenyl)-ethyl]-phenyl}-1H-pyrazole;
 1-phenyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;
 2-(4-chloro-phenyl)-N-methyl-2-[4-(1H-pyrazol-4-yl)-phenyl]-acetamide;
 N-methyl-2,2-bis-[4-(1H-pyrazol-4-yl)-phenyl]-acetamide;
 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;

20 {2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-ethyl-amine;
 4-{4-[1-(4-chloro-phenyl)-2-imidazol-1-yl-ethyl]-phenyl}-1H-pyrazole;
 methyl-{2-(4-phenoxy-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-amine;
 {2-(4-methoxy-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;
 methyl-{2-[4-(pyrazin-2-yloxy)-phenyl]-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-

25 amine;
 methyl-{2-phenoxy-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-amine;
 2-{(4-chloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methoxy}-ethylamine;
 4-{4-[1-(4-chloro-phenyl)-3-pyrrolidin-1-yl-propyl]-phenyl}-1H-pyrazole;
 4-{4-[3-azetidin-1-yl-1-(4-chloro-phenyl)-propyl]-phenyl}-1H-pyrazole;

30 methyl-{3-naphthalen-2-yl-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-amine;

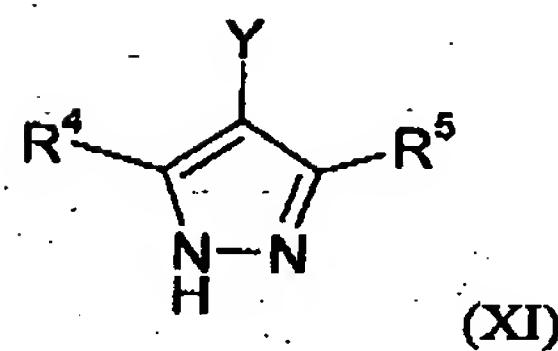
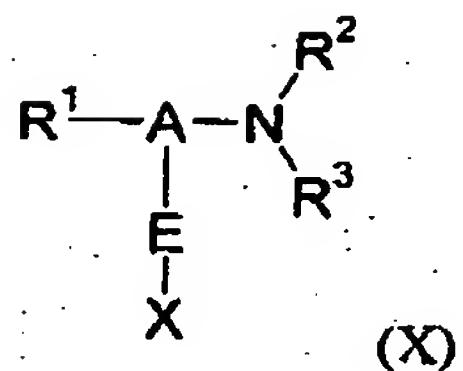
dimethyl-(4-{3-methylamino-1-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-phenyl)-amine;
(3-(4-fluoro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl)-methyl-amine;
4-{4-[4-(4-chloro-phenyl)-piperidin-4-yl]-phenyl}-1H-pyrazole-3-carbonitrile;
5 3-(4-phenoxy-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;
1-{(4-chloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-piperazine;
1-methyl-4-{phenyl-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-[1,4]diazepane;
{3-(3-chloro-phenoxy)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;
methyl-{2-phenyl-2-[6-(1H-pyrazol-4-yl)-pyridin-3-yl]-ethyl}-amine;
10 4-{4-[1-(4-chloro-phenyl)-3-imidazol-1-yl-propyl]-phenyl}-1H-pyrazole;
4-[4-(3-imidazol-1-yl-1-phenoxy-propyl)-phenyl]-1H-pyrazole;
4-{4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidin-4-yl}-phenol;
1-{(4-chloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-piperazine;
{2-(4-fluoro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;
15 {2-(3-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;
4-[4-(2-methoxy-ethoxy)-phenyl]-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;
4-[4-(3-methoxy-propoxy)-phenyl]-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;
3-(3,4-dichloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propionamide;
2-(4-{2-methylamino-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-phenoxy)-
20 isonicotinamide;
{2-(3-chloro-phenoxy)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-amine;
3-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamino}-propan-1-ol;
2-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamino}-ethanol;
3-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamino}-propan-1-ol;
25 2-{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamino}-ethanol;
{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-cyclopropylmethyl-
amine;
methyl-[2-[4-(1H-pyrazol-4-yl)-phenyl]-2-(4-pyridin-3-yl-phenyl)-ethyl]-amine;
4-{3-methylamino-1-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-phenol;
30 3-(4-methoxy-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;

4-(4-chloro-phenyl)-4-[4-(3-methyl-1H-pyrazol-4-yl)-phenyl]-piperidine;
2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-morpholine;
(4-{4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidin-4-yl}-phenoxy)-acetic acid;
(4-{4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidin-4-yl}-phenoxy)-acetic acid, methyl
ester;
4-{4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidin-4-yl}-benzonitrile;
{2-(4-chloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-amine;
1-(4-chloro-phenyl)-2-methylamino-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethanol;
2-amino-1-(4-chloro-phenyl)-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethanol;
10 4-(3,4-dichloro-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;
4-(3-chloro-4-methoxy-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;
4-(4-chloro-3-fluoro-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;
4-{4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidin-4-yl}-benzoic acid;
4-[4-(1H-pyrazol-4-yl)-phenyl]-1,2,3,4,5,6-hexahydro-[4,4']bipyridinyl;
15 3-(3-chloro-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;
2-methylamino-1-(4-nitro-phenyl)-1-[4-(1H-pyrazol-4-yl)-phenyl]-ethanol;
2-(3-chloro-4-methoxy-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;
2-(4-chloro-phenyl)-2-fluoro-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;
3-(3,4-dichloro-phenyl)-3-[6-(1H-pyrazol-4-yl)-pyridin-3-yl]-propylamine;
20 2-(4-chloro-3-fluoro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;
4-(2-chloro-3-fluoro-phenyl)-4-[4-(1H-pyrazol-4-yl)-phenyl]-piperidine;
1-{(3,4-dichloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-piperazine;
2-(3,4-dichloro-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethylamine;
{2-(3-chloro-4-methoxy-phenyl)-2-[4-(1H-pyrazol-4-yl)-phenyl]-ethyl}-methyl-
25 amine;
4-{4-[2-azetidin-1-yl-1-(4-chloro-phenoxy)-ethyl]-phenyl}-1H-pyrazole;
3-(3-chloro-4-methoxy-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propylamine;
{3-(3-chloro-4-methoxy-phenyl)-3-[4-(1H-pyrazol-4-yl)-phenyl]-propyl}-methyl-
amine;
30 1-{(3,4-dichloro-phenyl)-[4-(1H-pyrazol-4-yl)-phenyl]-methyl}-piperazine; or

C-(4-chloro-phenyl)-C-[4-(1H-pyrazol-4-yl)-phenyl]-methylamine;
and salts, solvates, tautomers and N-oxides thereof.

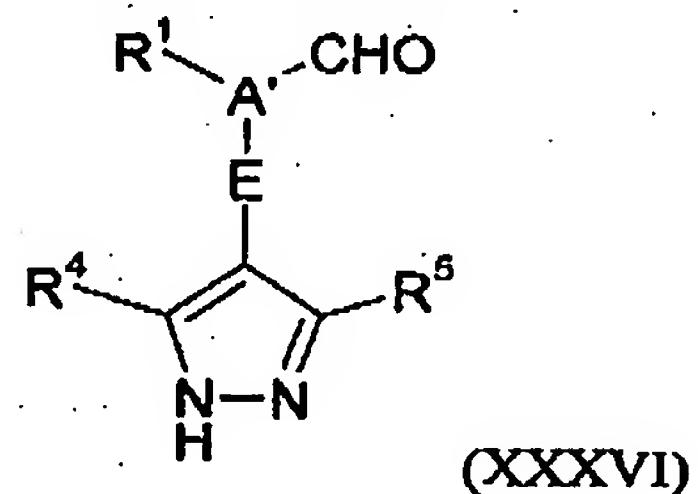
28. A compound according to any one of the preceding claims in the form of a salt, solvate (such as a hydrate), ester or N-oxide.
- 5 29. A compound as defined in any one of claims 1 to 28 for use in medicine; for example (a) for use in the prophylaxis or treatment of a disease state or condition mediated by protein kinase B; or (b) for use in the prophylaxis or treatment of a disease state or condition mediated by protein kinase A.
- 10 30. The use of a compound as defined in any one of claims 1 to 28 for:
 - (a) the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by protein kinase B; or
 - (b) the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition mediated by protein kinase A; or
 - (c) the manufacture of a medicament for the prophylaxis or treatment of a disease state or condition arising from abnormal cell growth;
 - (d) the manufacture of a medicament for the prophylaxis or treatment of a disease in which there is a disorder of proliferation, apoptosis or differentiation.
- 15 31. A pharmaceutical composition comprising a novel compound as defined in any one of claims 1 to 28 and a pharmaceutically acceptable carrier.
- 20 32. A process for the preparation of a compound of the formula (I) as defined in any one of claims 1 to 28, which process comprises:
 - (a) the reaction of a compound of the formula (X) with a compound of the formula (XI) or an N-protected derivative thereof:

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wherein A, E, and R¹ to R⁵ are as defined in any one of the preceding claims, one of the groups X and Y is selected from chlorine, bromine, iodine and trifluoromethanesulphonate, and the other one of the groups X and Y is a boronate residue, for example a boronate ester or boronic acid residue, in the presence of a palladium catalyst and a base;

5 (b) the reductive amination of a compound of the formula (XXXVI):



with HNR²R³ in the presence of a reducing agent; and optionally

10 (c) the conversion of one compound of the formula (I) into another compound of the formula (I).